ated high-pressure obstruction of the bladder from pelvic floor spasms; women with diabetes who have chills, fever, flank pain, and emphysematous pyelonephritis (diagnosed by finding intraparenchymal or perirenal gas on a plain film of the abdomen), a disease that carries a 43% mortality without early diagnosis and surgical drainage; and, finally, women who have pyelonephritis in the last trimester of pregnancy, a condition easily prevented by the diagnosis of a urinary tract infection in the first trimester, treated for three days with curative oral antimicrobial therapy, and followed by post-intercourse prophylaxis with nitrofurantoin or cephalexin.

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Premenstrual Syndrome

ALTHOUGH IT WAS FIVE DECADES AGO that Frank first described the premenstrual syndrome in the medical literature, little progress has been made in our understanding of this condition. As a result, family, friends, and physicians have often rejected the idea that it is a medical disorder and accused women with premenstrual symptoms of a lack of character, sanity, or moral fiber. This situation is not surprising, however, for until recently there has not been a clear definition or set of diagnostic criteria, a convincing theory for its etiology, or a proven approach to the therapy for the premenstrual syndrome.

Fortunately, a renewed interest in this phenomenon in the early 1980s by the medical and popular press has led to a serious attempt by many medical and social scientists to unravel the mysteries of this enigmatic problem. The first major article written by medical researchers in this country in the 1980s was by Reid and Yen.[1] They stated their belief that the premenstrual syndrome was a psychoneuroendocrine disorder—that is, a condition resulting from a disturbance of the neuroendocrinologic system but greatly influenced by psychosocial factors. Based on animal studies that showed a premenstrual decline in β-endorphins in the hypophyseal portal system and the similarity of many premenstrual symptoms to those that accompany an exposure to and withdrawal from narcotics, they proposed that a withdrawal from endogenous opiates may incite premenstrual symptoms. Unfortunately, studies of circulating endorphins in women with and without premenstrual symptoms proved contradictory. In the minds of many, however, their article legitimized the premenstrual syndrome as a medical disorder and stimulated the search for a common biochemical defect or a biological marker for the condition, a search that has not yet been successful.

While failure to discover a biochemical defect or biochemical marker has convinced some that the premenstrual syndrome is not a medical diagnosis at all, this failure probably reflects more our limited understanding of psychoneuroendocrinology and the limitations of our investigative tools and techniques than the nature of the syndrome.

Another problem facing clinicians and researchers had been the absence of a universally accepted set of diagnostic criteria. The 1980s, however, also produced a landmark article by Rubinow and Roy-Byrne that critically analyzed the methods of the past, established guidelines, and set standards for designing valid and reproducible studies.[2] Consequently, recent published studies of the premenstrual syndrome have been of higher quality and more believable than at any time in the past. As a result, many skeptical physicians are now taking an active interest in this issue. They recognize that distressing symptoms begin about 2 weeks before the menses and end within 24 hours after the menses begin. The most common physical symptoms are fatigue, headache, abdominal bloating, breast tenderness and swelling, and acne. Anxiety, hostility or anger, and depression occur in more than 94% of women with the syndrome. Many have psychological reactions such as guilt, decreased self-esteem, and shame; many also report notably disturbed family and work lives.

Another encouraging development has been the improved communication that has occurred between the psychologically oriented "camp" and the biologically oriented one of investigators and clinicians.[3] Whereas each camp previously gave lip service to the other, now each borrows concepts and methods from the other. Realizing that the premenstrual syndrome most likely is the result of both external (social) and internal (psychobiologic) factors, multidisciplinary teams have been formed to study, evaluate, and treat women with the disorder. This cooperation has led to new and effective treatment approaches, including various combinations of education, medication, and counseling—peer, individual, group, family, and marital. It now appears that a biopsychosocial model of the syndrome has come of age.[4]

Despite these dramatic advances in the field of "PMS-ology," we still have a long way to go. Scientists and health care providers, however, can be excited about the rapid rate at which insight into the nature of the syndrome is being gained. Most important, women with the disorder can be increasingly optimistic that in the future their care will be even more compassionate and effective.

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Advances in the Diagnosis and Treatment of Ovarian Cancer

OVARIAN CANCER is responsible for the death of more American women than cancers of the uterine cervix and corpus combined. It has been estimated that 19,000 new cases of ovarian cancer will be diagnosed in 1988 and that 12,000 of these women will eventually die of their disease.

Approximately 70% of all patients with epithelial ovarian cancer present with disease that has already spread beyond the confines of the pelvis to involve peritoneal sites throughout the abdomen. The role of aggressive cytoreductive surgery in the management of these patients remains

controversial. Several reports have now confirmed that patients with residual disease measuring less than 2 cm exhibit a higher rate of complete remission and a longer duration of survival than patients with bulky residual masses. Those who question the value of an aggressive surgical approach argue that a fundamental difference in tumor biology is responsible for the unfavorable prognosis in patients with bulky residual masses.

The resection of bulky abdominal disease poses a formidable challenge even to the most experienced and skillful surgeon. For this reason, it has been possible to achieve "optimal" cytoreduction in no more than 40% to 70% of cases. The results of a recent study offer some hope of improving these figures. In nine of ten elderly patients, an ultrasonic surgical aspirator was used to achieve cytoreduction of bulky peritoneal metastases to less than 0.5 cm. Procedures involving the aspirator took less than half the time required for conventional surgical techniques. Bowel resection was avoided in all but one patient, and no operative complications were attributed to the use of the device.

For many years, the primary focus of research in ovarian cancer has been the development of a more effective chemotherapeutic regimen for patients with advanced disease. Several prospective, randomized trials have now shown that the intravenous administration of cisplatin in combination with cyclophosphamide constitutes the most effective treatment for these patients. Chemotherapeutic regimens containing the two drugs have yielded objective response rates of 60% to 80%, complete response rates of 30% to 40%, and a median survival of 24 to 30 months. The addition of Adriamycin (doxorubicin hydrochloride) or other agents does not appear to enhance the effectiveness of the two-drug combination.

In patients with persistent disease at a second laparotomy, the likelihood of a response to additional intravenous chemotherapy is less than 20% and the median survival is only six months. Ovarian cancer, however, is uniquely suitable for an alternative approach to drug administration. The direct intraperitoneal instillation of a chemotherapeutic agent exposes residual tumor nodules to an extremely high drug concentration as compared with systemic levels, making it possible in theory to enhance the drug's therapeutic index. In a recent study of intraperitoneal chemotherapy for residual disease at a second laparotomy, a cisplatin-based combination yielded a median survival of more than four years in patients whose disease measured less than 2 cm. Unfortunately, patients with more extensive residual disease did not benefit to the same degree.

Localized ovarian cancer is usually asymptomatic. Until recently, the only potential screening test for asymptomatic disease was a vaginal examination. Discovery of the CA-125 antigen and improvements in the technique of real-time ultrasonography have raised the possibility that an effective program for early detection can be developed. The CA-125 antigen is a glycoprotein that is expressed by more than 80% of nonmucinous epithelial ovarian cancers. Real-time ultrasonography is an accurate method of measuring ovarian volume.

In a recent study to determine the feasibility and specificity of multimodal screening, serum CA-125 levels were determined in 1,010 postmenopausal women. Ovarian ultrasonography, a less specific and more expensive test, was carried out in the 30 women with CA-125 levels greater than 30 units per ml. Only three of these women with elevated CA-125 levels had abnormal ultrasound scans. One of them was found to have stage I ovarian cancer, while the other two proved to have benign pelvic abnormalities. The specificity of the multimodal screening program was therefore 99.8%. To determine whether such a screening program is of real value would first require additional studies to define the sensitivity in patients with localized disease. Ultimately, it would be necessary to do a randomized, controlled trial to show a reduction in mortality.

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Topical Retinoic Acid, Aging, and the Skin

AMERICANS ARE CONTINUALLY BARRAGED by commercial images that promote gnawing anxiety about the normal consequences of aging. A disproportionate share of this dissatisfaction has focused on the perceived ravages of aging on the skin and its appendages. Much of this attention has been useful; for example, an increased use of sunscreens should slow the alarming recent increase in cases of skin carcinoma and melanoma. On the other hand, much of the anxiety about aging is not endogenous but fueled by aggressive marketing targeted at a population evermore dependent on passively received, idealized images for its perception of normal. Whether this has been beneficial is certainly debatable, particularly if the price is despair and depression. Physicians, traditionally the last bastion of skepticism and independent thinking, likewise are becoming increasingly dependent on passively dispensed information—videocassettes, direct mail advertising, drug company-sponsored speakers, and throwaway journals compiled by nonmedical journalists—because they, too, are part of a society that reads and thinks less. By obtaining their information through these routes, physicians knowingly or unwittingly become salespeople, themselves extensions of a marketing network, corrupting their primary responsibility as patients' advocates.

Nevertheless, the phenomenon is upon us. Where before monarchs, poets, and commoners alike awaited their death knell from an early age with each serious illness, we can now reasonably expect longevity, while at the same time our skin will increasingly be besieged by the electromagnetic consequences of a careless disregard of a deteriorating atmosphere and increased sun exposure due to expanded leisure time and Sunbelt migration patterns.

A veritable smorgasbord of cutaneous offerings awaits those in search of the font of youth: body recontouring by removal (plastic surgery or liposuction), or augmentation (collagen, fat, or silicon implantation), hair-growth potions of still-unproven value, "cosmetics of the future," and topical retinoids. Although all of these approaches merit separate examination of their relative virtues and demerits, it seems